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A resurgence of Sleeping sickness amidst the COVID-19 pandemic: Correspondence

Human African trypanosomiasis (HAT), also called as Sleeping sickness is an old vector-borne (fly of the genus Glossina) Neglected Tropical Disease with a massive impact on public health in entire Africa. It is caused by a flagellated protozoan parasite *Trypanosoma brucei,* which is categorised under five subspecies namely 1.) *T. b. brucei,* 2.) *T. b. gambiense*, 3.) *T. b. rhodesiense* 4.) *T. b. equiperdum* and 5.) *T. b. evansi.* Of all, 95% of HAT cases are caused by *T. brucei gambiense*, especially in Central and Western Africa (North Uganda Angola, Gambia, Guinea, Mali, Niger, Nigeria, Congo, and South Sudan). *T. brucei rhodesiense* is responsible for 12% of registered cases in East Africa (Malawi, Tanzania, South Uganda, Zimbabwe, and Zambia.) [1] Sporadic cases have been reported from non-endemic regions also like Europe, the USA, South Africa, and China mainly because of alliances and commercial links with disease-endemic countries [2]. The parasite has a predilection to infect central nervous system as disease progresses clinically, increasing its morbidity and mortality profile [1].

Table 1. And 2. Show the overall number of reported HAT cases (by *T.b. gambiense,* and *T.b. rhodesiense* respectively). The incidence of Sleeping sickness has declined over years with more than 2000 cases by T.b. *gambiense* reported in the year 2015 to 700 cases in the year 2021. Africa has witnessed many epidemics of Sleeping Sickness over the last century: first in 1896–1906 in the Democratic Republic of Congo (DCR) and Uganda; second in the year 1920 in almost whole of Africa and the most recent which started in the year 1970 and lasted till the year1990. By the mid-1960s, cases were less than 5000 cases in the whole continent of Africa, following which monitoring was relaxed. Consequently, the cases again peaked at epidemic proportions by the year 1970 marking the start of the third epidemic. Since the number of new HAT cases reported between 2000 and 2012 dropped considerably as a result of the World Health Organisation (WHO)-led efforts, elimination of this NTD was targeted by 2020 and interruption of transmission (i.e. zero cases) by 2030. This decline in the incidence continued in 2019 and 2020 also [3]. In the year 2022, a total of 99 cases have been registered from Democratic Republic of Congo (DCR) and 11 from Brazil. Over the years, DCR has been the worst affected region. No data of HAT cases by *T.b. rhodesiense* have been registered in the year 2022, yet 55 cases in the year 2021 have been documented with a majority of cases from Malawi [4].

HAT is currently endemic in a total of 36 sub-Saharan African countries where tsetse flies are found. The affected population chiefly has agriculture, fishing, and animal husbandry as their sole source of livelihood. The two subspecies have entirely different manifestations. *T. brucei gambiense* causes a chronic infection, with no signs and symptoms for a longer duration, and by the time evident symptoms manifest, the patient's central nervous system (CNS) is already affected. Infection with *T. b. rhodesiense*manifests acutely and the disease develops rapidly to involve the CNS. Uganda is only region to have prevalence of both forms of the disease [3].

The infection progress through three phases 1.) Cutaneous 2.) Hemo-lymphatic and 3.) Meningoencephalitic. The cutaneous phase happens after parasite entry, a chancre might develop. In the hemo-lymphatic phase, the symptoms can be non-specific like headache, anorexia, pruritus, generalized malaise and weakness, weight loss, and lymphadenopathy (axillary, cervical, epitrochlear, and supraclavicular). The second phase is followed by CNS manifestations which are severe in *T. brucei gambiense* such as severe headache, insomnia, mood swings, tremors, gait disturbances, involuntary movements of the upper and lower limbs and trunk, abnormal muscular tones, fasciculation, akinesia, speech disorders, cranial nerve disorders, instability, attention deficit, and apathy. Although *T. brucei rhodesiense* has a shorter incubation period yet it presents with high and persistent parasitemia, rapid progression to the meningoencephalic phase as compared to other species and lymphadenomegaly is uncommon [1].

Thorough history should be sought for any travel to endemic areas as the vector has defined geographical spread. Pathological investigation reveals anaemia and increased erythrocyte sedimentation rate because of inflammation, hypoalbuminemia, and hypergammaglobulinemia. The parasite can be identified in the blood, lymph node aspirate, chancre, or CSF via microscopy. Prompt diagnosis is of utmost importance to prevent disease progression to the meningoencephalitic phase and to control the distribution of the parasite to the vector, which can in turn limit the spread of the infection [1]. Other good diagnostic methods such as rapid lateral flow devices, recombinant polymerase amplification, and loop mediated isothermal amplification are still not widely. Recently, new CRISPR-Cas based innovative diagnostic technology has been applied to confirm the diagnosis of HAT with favourable results, but use is limited to some research laboratories. The use of computerized tomographic scan and magnetic resonance imaging is limited because as these can only detect changes in severe cases [1].

Pentamidine and suramin are the oldest used drugs for hemo-lymphatic stage *T. b. gambiense* HAT and *T. b. rhodesiense* HAT, respectively. Combination therapy of nifurtimox and intravenous eflornithine is used for treatment of the meningoencephalitic phase since the year 2009. Recently introduced fexinidazole is used as an oral drug for treatment for *T. b. gambiense* HAT, it has been a boon in the treatment of HAT and a major step forward in elimination efforts by 2030. For *T. b. rhodesiense*-HAT, arsenic melarsoprol is used for the meningoencephalitic stage, which is highly toxic [5]. After adequate treatment, 90%–95% of cases in the hemo-lymphatic and meningoencephalic phase can be cured. There is still no vaccine available for HAT [1]. To prevent spread of HAT, detecting new cases is crucial since these individuals are reservoirs and may infect all tsetse flies that they come into their contact. The following measures can be taken 1). Early detection and screening of at-risk populations 2). Vector control through use of traps,

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Table 1
Total number of reported cases of Sleeping sickness caused by *T.b. gambiense* as per WHO Global health observatory [4].

Country	Year							
	2022	2021	2020	2019	2018	2017	2016	2015
Angola	Data not available	174	33	30	79	18	20	35
Burkina Faso	Data not available	0	0	0	0	0	0	1
Cameroon	Data not available	11	2	20	7	5	6	6
Central African Republic	Data not available	44	39	86	57	76	101	147
Chad	Data not available	15	17	16	12	28	54	67
Congo	Data not available	18	15	17	24	15	18	36
Côte d'Ivoire	Data not available	1	0	1	2	3	0	3
DR Congo	88	425	395	613	660	1100	1768	2347
Equatorial Guinea	Data not available	3	1	3	4	4	3	0
Gabon	Data not available	18	11	8	16	9	10	9
Ghana	Data not available	0	0	0	0	0	0	0
Guinea	Data not available	28	36	69	74	139	108	29
Nigeria	Data not available	0	0	0	0	0	1	0
South Sudan	Data not available	10	15	11	17	12	17	45
Uganda	Data not available	0	1	2	1	0	4	4
Brazil	11	Data not available	Data not available	Data not available	Data not available	Data not available	Data not available	Data not available
Total	99	747	565	876	953	1409	2110	2729

Table 2
Total number of reported cases of sleeping sickness caused by *T.b. rhodesiense* as per WHO Global health observatory [4].

Country	Year							
	2022	2021	2020	2019	2018	2017	2016	2015
Malawi	No data	49	89	91	15	7	35	30
Uganda	No data	2	2	5	4	13	10	28
United Republic of Tanzania	No data	1	1	3	0	3	4	2
Zambia	No data	3	6	15	5	3	4	9
Zimbabwe	No data	0	0	2	0	1	1	3
Total	No data	55	98	116	24	27	54	72

nets, curtains, and repellents for individual protection, 3). Awareness and education must be provided to all living in and travelling to endemic regions [1].

In the year 2000, WHO founded public-private partnerships to strengthen control and surveillance program, providing support to the endemic countries in the form of the free of cost supply of antiparasitic drugs and technical assistance. In the year 2009, WHO set up a specimen submission database at the Institute Pasteur of Paris, for promoting research in development of new and cheaper diagnostic methods for HAT. In the year 2014, a coordination network was established to strengthen efforts to eliminate HAT. The African Union in coordination with United Nation's agencies have promoted the 'Programme against African Trypanosomiasis' to support vector and disease control activities [3]. When untreated, the disease is lethal and the available therapeutics have poor cure rate, are difficult to administer, and toxic, especially in the meningoencepahlitic phase. The development of vaccines and new pharmaceutical products with better toxicity profiles and improvised effectiveness is of prime importance to eliminate HAT and is the need of the hour.

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